

## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after allowance or after an Office action under *Ex Parte Quayle*, 25 USPQ 74, 453 O.G. 213 (Comm'r Pat. 1935). Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 9/11/2009 has been entered.

Receipt is also acknowledged of the amendments and remarks filed 12/22/2008.

### ***Information Disclosure Statement***

Acknowledgement is made of applicant's submitting an information disclosure statement on 9/11/2009. With the exception of those references which have been lined out, the submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the examiner.

References labeled CD, CE and CF on the IDS filed 9/11/2009 have been lined out because these references were cited on PTO form 892 on 8/1/2008 by the Examiner. Accordingly, these references are redundant and were lined out to prevent their being printed twice on the face of the patent should a patent be granted for this application.

### EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

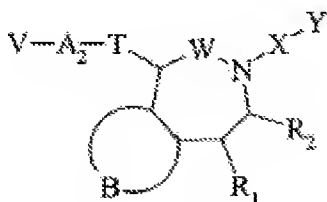
Authorization for this examiner's amendment was given in a telephone interview with Gabriel McCool on 10/7/2009.

**Cancel claims 5, 7, and 10-14.**

### REASONS FOR ALLOWANCE

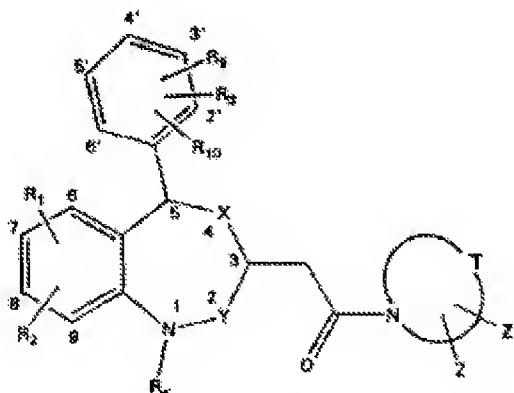
The following is an examiner's statement of reasons for allowance: The instantly claimed compounds are novel and non-obvious over the prior art. The Examiner has determined that the closest prior art in respect to the compounds claimed is WO 02/057258 (as per Applicant's IDS dated 8/9/2006) and WO 97/48701 (made of record in the Office action dated 8/1/2008).

WO 02/057258 teaches compounds of the following general structure which are useful as farnesyltransferase inhibitors:



These compounds have the same core structure as the instantly claimed compounds, and differ from the instant compounds only in the X-Y chain off the nitrogen.

WO 97/48701 teaches compounds of the following general structure which are useful as squalene synthetase inhibitors:



These compounds differ from the instant compounds in the atoms in the 7-membered ring (specifically the position of the nitrogen and the presence of X, which is O or S). The peripheral groups, and their positions meet those of the instant application.

Neither reference alone teaches the instantly claimed compounds and the different core structures disclosed in WO 02/057258 and WO 97/48701 prevents their combination for an obviousness-type rejection.

Applicant's disclosure states that the instantly claimed compounds are useful as squalene synthetase inhibitors. The specification fails to provide inhibition data for specific compounds, but generally states that the instant compounds, are squalene synthetase inhibitors with an IC<sub>50</sub> value of at least 20  $\mu$ M (page 80, line 27). As discussed in the Office action dated 8/1/2008, Pandit et al. (Journal of Biological Chemistry, "Crystal Structure of Human Squalene Synthase" vol. 275(39) 2000, 30610-30617) teaches the crystal structure of human squalene synthase. The crystal structure of the protein with three different inhibitor complexes is described (page 30614, final paragraph and figures 6 a-c). The inhibitors of figures 6a and 6c, CP-320473 and CP-

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424677 respectively show  $IC_{50}$  values of 56 and 32 nM respectively. The inhibitor of figure 6b, CP-458003, an analog of CP-320473, is smaller and thus fills a smaller portion of the binding pocket and as a result is less potent and shows  $IC_{50}$  values around 30  $\mu$ M, much like the instant compounds. Pandit teaches that the inhibitor binding pockets are largely hydrophobic and have the ability to change size and shape in order to accommodate different ligands. This shape change is accomplished through rotations of the Phe<sup>54</sup> and Tyr<sup>73</sup> side chains as well as through backbone rotations (page 30616, fig. 6 description, also the final portion of the second paragraph of the second column on page 30616).

With the knowledge that structurally similar 7-membered ring compounds taught in WO 02/057258, WO 97/48701 and in Pandit show squalene synthase inhibition along with the fact that the squalene synthase binding pocket is relatively non-discriminatory, one of ordinary skill in the art at the time of the instant invention would expect the instantly claimed compounds to exhibit squalene synthase inhibition activity.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

### ***Conclusion***

Claims 1-4, 8-9 are allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kortney Klinkel whose telephone number is (571)270-5239. The examiner can normally be reached on Monday-Friday 8am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau can be reached at (571)272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

KLK

/Sharmila Gollamudi Landau/

Supervisory Patent Examiner, Art Unit 1611